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Body mass index, dialysis modality, and survival: Analysis of the United States Renal Data System Dialysis Morbidity and Mortality Wave II Study

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Body mass index, dialysis modality, and survival: Analysis of the United States Renal Data System Dialysis Morbidity and Mortality Wave II Study.

Background. The impact of obesity on survival in end-stage renal disease (ESRD) patients as related to dialysis modality (i.e., a direct comparison of hemodialysis with peritoneal dialysis) has not been assessed adjusting for differences in medication use, follow-up ≥2 years, or accounting for changes in dialysis modality.

Methods. We performed a retrospective cohort study of the United States Renal Data System (USRDS) Dialysis Morbidity and Mortality Wave II Study (DMMS) patients who started dialysis in 1996, and were followed until October 31 2001. Cox regression analysis was used to model adjusted hazard ratios (AHR) for mortality for categories of body mass index (BMI), both as quartiles and as ≥30 kg/m^2 vs. lower. Because such a large proportion of peritoneal dialysis patients changed to hemodialysis during the study period (45.5%), a sensitivity analysis was performed calculating survival time both censoring and not censoring on the date of change from peritoneal dialysis to hemodialysis.

Results. There were 1675 hemodialysis and 1662 peritoneal dialysis patients. Among hemodialysis patients, 5-year survival for patients with BMI ≥30 kg/m^2 was 39.8% vs. 32.3% for lower BMI ($P < 0.01$ by log-rank test). Among peritoneal dialysis patients, 5-year survival for patients with BMI ≥30 kg/m^2 was 38.7% vs. 40.4% for lower BMI ($P > 0.05$ by log-rank test). In adjusted analysis, BMI ≥ 30 kg/m^2 was associated with improved survival in hemodialysis patients (AHR 0.89; 95% CI 0.81, 0.99; $P = 0.042$) but not peritoneal dialysis patients (AHR = 0.99; 95% CI, 0.86, 1.15; $P = 0.89$). Results were not different on censoring of change from peritoneal dialysis to hemodialysis.

Conclusion. We conclude that any survival advantage associated with obesity among chronic dialysis patients is significantly less likely for peritoneal dialysis patients, compared to hemodialysis patients.

In contrast to the general population, obesity [defined as a body mass index (BMI) ≥30 kg/m^2] has generally been associated with improved survival among chronic hemodialysis patients, even after adjusting for differences in dialysis adequacy [1–6]. However, previous studies limited to peritoneal dialysis patients have so far yielded conflicting results regarding an association between obesity and survival [7, 8]. Whether these discrepancies are due to differences in populations studied, methodology, sample size, or duration of follow-up has not been determined. The clinical importance of obesity is underscored by its rapidly increasing prevalence in both the general [9] and dialysis populations [10]. Obesity is also more common among African Americans [9], who are overrepresented in the chronic dialysis population. Among dialysis patients, obese African Americans may have improved survival compared to obese Caucasians [11, 12]. A previous study, currently available only in abstract form [abstract; Stack AG, et al, *Am J Kidney Dis* 41:A35 (abstract #95), 2003], has directly assessed the association between BMI and survival between peritoneal dialysis and hemodialysis patients. However, information on factors recently shown to have significant associations with survival, such as use of 3-hydroxy-3-methylglutaryl

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Key words: obesity, body mass index, peritoneal dialysis, hemodialysis, survival, mortality.

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coenzyme A (HMG-CoA) reductase inhibitors [13], calcium channel blockers [14], serum cholesterol levels [15], and pulse pressure [16] were not available. The optimal dialysis modality for obese patients who reach end stage renal disease (ESRD), other than renal transplantation, [17] has also not been determined.

To determine whether obesity has a significantly different association with survival in hemodialysis patients compared to peritoneal dialysis patients, we conducted a historical cohort study of the United States Renal Data System (USRDS) Dialysis Morbidity and Mortality Wave II (DMMS) database. Data collection was conducted as a true prospective study of patients starting dialysis therapy in 1996, with comparable numbers of hemodialysis and peritoneal dialysis patients to facilitate comparisons between dialysis modalities. The objective of the study was to determine whether the association between obesity and survival differed for hemodialysis vs. peritoneal dialysis patients, and whether obese patients had differing survival with one modality vs. another. The null hypothesis was the association between BMI and survival was not significantly different in hemodialysis patients compared to peritoneal dialysis patients.

METHODS

Subjects

A retrospective cohort study of the USRDS DMMS Wave II was performed; details of the studies performed by the USRDS are described elsewhere [10]. Briefly, the USRDS collects demographic and clinical data on patients who have survived more than 90 days on dialysis. DMMS Wave II was a prospective cohort study that included all eligible patients initiating peritoneal dialysis and a 20% random sample of patients initiating hemodialysis in 1996 and early 1997. This cohort was designed to enable comparison of hemodialysis with peritoneal dialysis patients. Since only a fraction of patients from the year 1997 were available, the present analysis included only patients whose first date of ESRD was in 1996. Other details of the demographics and extraction of DMMS Wave II have been described in other studies [18].

Data collection

As part of the USRDS cohort study, dialysis unit personnel performed chart reviews to obtain baseline and follow-up patient data. Selected data for each patient at the start of the study were as listed in Table 1. For peritoneal dialysis patients, BMI was calculated from height at the start of the study period and the "dry weight," as indicated in the study questionnaire (which implied but did not explicitly specify whether this meant without a fluid dwell). For hemodialysis patients, weight for the calculation of BMI was obtained from the average of three postdialysis weights (from the three most recent sessions prior to the study start) since this is generally considered a better approximation of patient's estimated dry weight. In addition, a maximum of 15 medications prescribed to each patient at the study start date (day 60 of dialysis) were recorded in the DMMS Wave II database. From this list, the use of angiotensin-converting enzyme (ACE) inhibitors, beta blockers, calcium channel blockers, HMG-CoA reductase inhibitors, and aspirin was determined. Carvedilol was approved for use by the federal Food and Drug Administration (FDA) in 1997 and was therefore not assessed. Pre- and postdialysis blood pressures, and intradialytic weight gains (hemodialysis patients only) were averaged for three values determined after the study start. Timing of blood pressure relative to peritoneal dialysis exchanges was not specified. For this reason, pulse pressure was calculated from predialysis blood pressure readings only.

Outcome measurements

Survival status was linked to the DMMS Wave II data from the USRDS patients Standard Analysis File (SAF) via unique patient identifiers assigned by the USRDS. The date and cause of death listed in a patient's SAF was obtained from a form submitted to the USRDS by the patient's nephrologist (formerly Health Care Finance Authority, HCFA 2746). Patient survival status was complete through October 31, 2001.

Although the DMMS Wave II data were collected at day 60 after the first dialysis session, mortality was not uniformly reported until 90 days after the first dialysis session. Therefore, survival time was calculated as the time from 90 days after the date of the first ESRD treatment until the date of death, censored for the end of the study or loss to follow-up. Although neither hemodialysis nor peritoneal dialysis was independently associated with survival, we performed a sensitivity analysis by calculating survival time in two ways and measuring the effects separately: (*1*) censored upon change from either peritoneal dialysis to hemodialysis or from hemodialysis to peritoneal dialysis, and (*2*) not censored for such changes. However, renal transplantation was significantly associated with mortality. Since the assumptions of survival analysis prohibit censoring on variables that are significantly associated with survival, due to possible introduction of bias [19], renal transplantation was modeled as a time-dependent covariate, similar to previous analyses of this database [11, 12].

Statistical analysis

Univariate analysis was performed with chi-square testing for categorical variables and Student *t* test for continuous variables. Continuous variables that did not have a normal distribution, namely serum parathyroid hormone (PTH) levels, were analyzed using the

Table 1. Factors assessed in end-stage renal disease (ESRD) patients, Dialysis Morbidity and Mortality Wave II (DMMS Wave II), 1996

	Hemodialysis	Missing	Peritoneal dialysis	Missing
Number	1675		1662	
Body mass index *kg/m²*	26.3 ± 6.4	137 (8.2)	26.4 ± 5.5	39 (2.3)
Body mass index ≥*30 kg/m²*	352 (22.9)		357 (22.0)	
Body mass index ≤*19 kg/m²*	120 (7.2)		89 (5.4)[a]	
Mean age *years*	61.7 ± 15.6	5 (0.3)	56.3 ± 15.7[b]	10 (0.6)
Male	893 (53.3)	0	890 (53.5)	0
African American	565 (33.7)	0	358 (21.5)[a]	0
Ever transplanted (yes/no)	147 (8.8)	Assumed 0	311 (18.7)[a]	Assumed 0
Diabetes	847 (51.6)	33 (2.0)	808 (49.7)	35 (2.1)
Coronary heart disease	580 (37.6)	134 (8.0)	503 (32.3)[a]	107 (6.4)
Congestive heart failure	640 (40.8)	106 (6.3)	502 (31.8)[a]	82 (4.9)
Peripheral vascular disease	309 (20.0)	129 (7.7)	251 (16.1)[a]	100 (6.0)
Malnutrition	212 (13.9)	150 (9.0)	232 (15.4)	156 (9.4)
Smoking (current)	216 (13.8)	108 (6.4)	236 (15.3)	119 (7.2)
Continuous variables				
Serum albumin *g/dL*	3.48 ± 0.58	117 (7.0)	3.41 ± 0.60[b]	187 (11.3)
Cholesterol *mg/dL*	180.0 ± 45.4	0	205.5 ± 51.8[b]	0
Hematocrit %	29.8 ± 5.7	45 (2.7)	31.3 ± 6.5[b]	39 (2.3)
Serum bicarbonate *mg/dL*	20.9 ± 6.6	117 (7.0)	23.7 ± 6.7[b]	179 (10.8)
Pulse pressure (using predialysis values for hemodialysis patients) *mm Hg*	73.1 ± 19.7	26 (1.6)	62.1 ± 20.0[b]	33 (2.0)
Medications				
Angiotensin-converting enzyme inhibitor	355 (21.2)	Assumed 0	410 (24.7)[a]	Assumed 0
Statin (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor)	100 (6.0)	Assumed 0	174 (10.5)[a]	Assumed 0
Calcium channel blocker	817 (48.8)	Assumed 0	862 (51.3)	Assumed 0
Aspirin	314 (18.7)	Assumed 0	309 (18.6)	Assumed 0
Beta blocker	290 (17.3)	Assumed 0	348 (20.9)[a]	Assumed 0
Functional status				
Independent walking	1380 (83.3)	19 (1.1)	1538 (93.3)[a]	13 (0.8)

In column one, data given as the number (% of total) or mean ± one standard deviation. Values determined at 60 days after the start of dialysis.
[a] $P < 0.05$ by chi-square, peritoneal dialysis vs. hemodialysis; [b] $P < 0.05$ by Student t test, peritoneal dialysis vs. hemodialysis in mm Hg.

Mann-Whitney test. Missing values for continuous variables were analyzed in two ways: both as truly missing and as set to the mean of the variable, while missing values for categorical variables were presumed to be absent, as in previous investigations of the USRDS [20]. Kaplan-Meier analysis was used to plot unadjusted survival of peritoneal dialysis and hemodialysis patients by categories of BMI (as categories of ≥30 kg/m^2 vs. lower and as quartiles; narrower categories of BMI were not practical due to sample size limitations).

Variables with $P < 0.10$ in univariate analysis for an association with mortality were entered into multivariate analysis as covariates. An exception was made for factors thought to have a clinical reason to be associated with mortality, in accordance with established epidemiologic principles [21]. These included ACE inhibitors, calcium channel blockers, beta blockers, BMI, race, gender, coronary heart disease, hematocrit, and ESRD network (to assess for regional differences). Information on urine volume was missing for the majority of patients, and thus calculation of residual renal function was not performed. Likewise, dialysis adequacy was not comparable between patients undergoing hemodialysis vs. patients on peritoneal dialysis.

Stepwise Cox proportional hazards model for censored survival data was used to assess the association between baseline factors and time to mortality, independent of other predictors. Adjustment variables were chosen for the multivariate regression model based on the possibility that the covariate of interest was either significant in univariate analysis or had clinical evidence of a relationship to the risk of mortality, as above. Log-log plots were inspected to verify the existence of proportional hazards. In Cox regression of analysis of the cohort of USRDS patients who started dialysis in 1996 who had valid BMI, covariates in analysis included BMI (as categories of ≥30 kg/m^2 vs. lower and as quartiles), patient age, race, gender, diabetes as a causes of renal failure (yes/no), and a history of congestive heart failure, ischemic heart disease, peripheral vascular disease, pulse pressure, ability to walk independently, quartiles of serum albumin and cholesterol levels, presence of malnutrition (subjective impression), renal transplantation (as a time-dependent variable), and use of aspirin, ACE inhibitors, beta blockers, calcium channel blockers, and HMG-CoA reductase inhibitors. A separate stratified analysis was performed of factors associated with survival for patients with BMI ≥30 kg/m^2.

RESULTS

A total of 4065 patients were included in the DMMS Wave II cohort. Of these, 3621 patients had valid dates for starting dialysis in 1996. From this cohort, 3374 had sufficient information to calculate follow-up times. Of the 1662 patients who started out on peritoneal dialysis, 757 (45.5%) changed to hemodialysis for 60 consecutive days at least once during the study period. The mean time to the earliest switch from hemodialysis to peritoneal dialysis was 2.05 ± 1.30 years. The rate of change to hemodialysis from peritoneal dialysis was constant over time. A change from peritoneal dialysis to hemodialysis was more frequent among patients with a higher quartile of BMI (47.1% among those in the highest quartile of BMI vs. 41.8% for those in the lowest quartile of BMI), but this was not statistically significant ($P = 0.64$ by chi-square). Among the 1675 hemodialysis patients, 71 (4.2%) changed to peritoneal dialysis for 60 days at least once during the study period. After exclusion of missing values and values not thought to be biologically plausible, BMI could be calculated for 91.8% of hemodialysis patients and for 97.7% of peritoneal dialysis patients.

Characteristics of the study population are summarized in Table 1. In unadjusted analysis, there were many differences between hemodialysis and peritoneal dialysis patients despite the attempts of the DMMS Wave II database to create a "matched" population by dialysis modality. At 60 days after the start of dialysis, peritoneal dialysis was significantly associated with a lower frequency of African American patients, younger age, increased rate of renal transplantation, decreased prevalence of coronary heart disease and congestive heart failure, lower prevalence of stroke, peripheral vascular disease, left ventricular hypertrophy on ECG, and cancer, decreased use of erythropoietin, and higher levels of cholesterol, hematocrit, bicarbonate, lower pulse pressure, and higher rates of use of ACE inhibitors, HMG-CoA reductase inhibitors, and beta blockers. However, BMI was not significantly different between hemodialysis and peritoneal dialysis patients when assessed as a continuous variable. Values for serum calcium, phosphorous, and PTH were not significantly different between hemodialysis and peritoneal dialysis patients and have been reported previously [19].

Figure 1 shows a histogram of BMI among hemodialysis patients, with results similar to those reported previously [22]. Figure 2 shows a histogram of BMI among peritoneal dialysis patients. In comparison, the BMI distribution among hemodialysis patients showed more leftward skewing (skew 0.96) compared to peritoneal dialysis patients (skew 0.81).

Among hemodialysis patients, 1100 (65.7%) died during the study period. Censoring hemodialysis patients who later changed to peritoneal dialysis reduced the total number of deaths to 1064 (63.5%). Figure 3 shows a

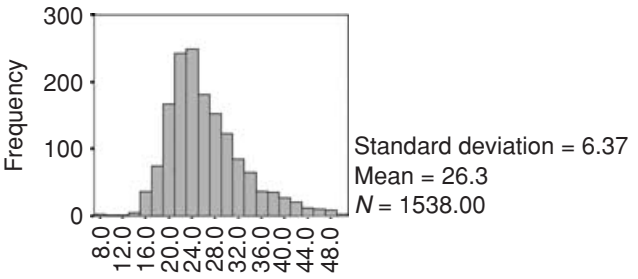

Fig. 1. Histogram of body mass index (BMI) of hemodialysis patients with valid BMI.

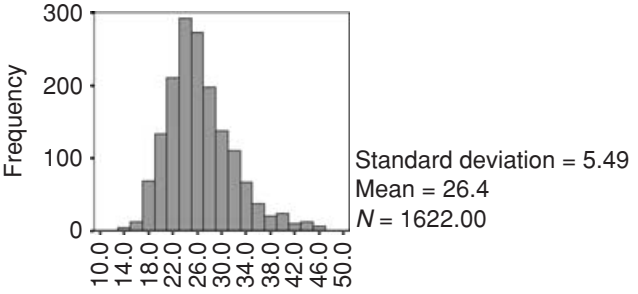

Fig. 2. Histogram of body mass index (BMI) of peritoneal dialysis patients with valid BMI.

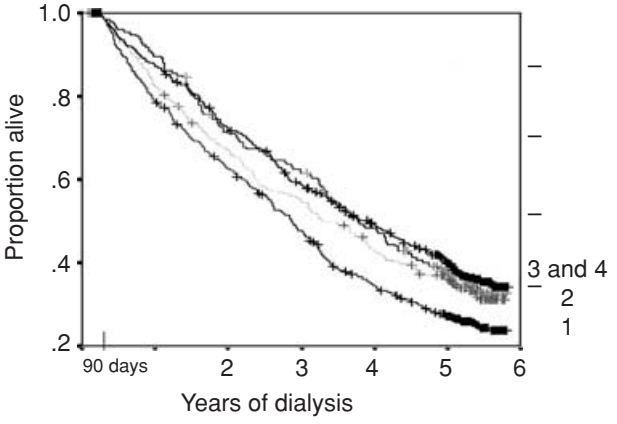

Fig. 3. Kaplan-Meier plot of patient survival by quartile of body mass index (BMI) in kg/m^2, hemodialysis patients only, Dialysis Morbidity and Mortality Wave II (DMMS Wave II). Patients in the lowest two quartiles of BMI consistently had the worst survival, while those in the highest two quartiles had equivalent survival after approximately 2 years. Quartiles of BMI = 4 (>29.9), 3(>25.0–29.9), 2(21.9–24.9), 1(<21.9). Quartile of BMI 1 $P < 0.01$ by log-rank test vs. highest quartile.

Kaplan-Meier plot of survival time by quartile of BMI for hemodialysis patients. As shown, hemodialysis patients in the lowest quartile of BMI consistently had the worst survival during the course of the study. However, early in the study, hemodialysis patients in the third quartile of BMI had the best survival, while after 2 years survival for hemodialysis patients in the third and fourth quartiles of BMI became equivalent. However, survival was consistently higher for hemodialysis patients with BMI

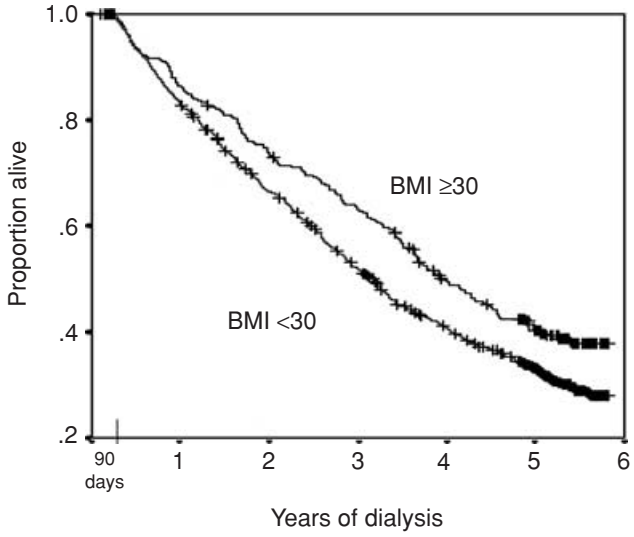

Fig. 4. Kaplan-Meier plot of patient survival by body mass index (BMI) $\geq$ 30 kg/m^2 or less, hemodialysis patients only, Dialysis Morbidity and Mortality Wave II (DMMS Wave II). Patients with BMI $\geq$ 30 kg/m^2 had improved survival compared to those with lower BMI, $P < 0.01$ by log-rank test.

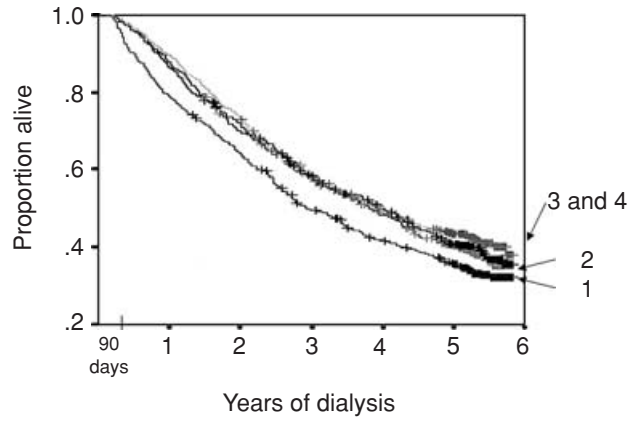

Fig. 5. Kaplan-Meier plot of patient survival by quartile of body mass index (BMI) in kg/m^2, peritoneal dialysis patients only, Dialysis Morbidity and Mortality Wave II (DMMS Wave II). Patients in the lowest quartile of BMI had the lowest survival, but this was not statistically significant ($P = 0.09$ by Log Rank test vs. highest quartile). Quartiles of BMI = 4 (>29.5), 3(>25.7–29.5), 2(22.4–25.7), 1(<22.4).

$\geq$30 kg/m^2 (vs. lower BMI) over time (Fig. 4) ($P < 0.01$ by log-rank test).

Among peritoneal dialysis patients, 989 (59.5%) died during the period of the study. Censoring of peritoneal dialysis patients who later changed to hemodialysis reduced the total number of deaths to 585 (35.2%). However, the graphic relationship between BMI and death did not change, regardless of censoring strategy. For peritoneal dialysis patients, Figure 5 (which did not censor on change from peritoneal dialysis to hemodialysis) and Figure 6 (which did censor on change from peritoneal dialysis to hemodialysis) show a similar Kaplan-Meier

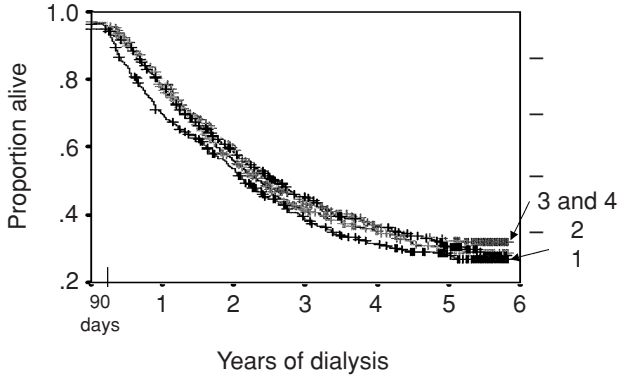

Fig. 6. Analysis from Fig. 5 censored for change to hemodialysis showed a lower rate of death overall, but a similar relationship between body mass index (BMI) and survival.

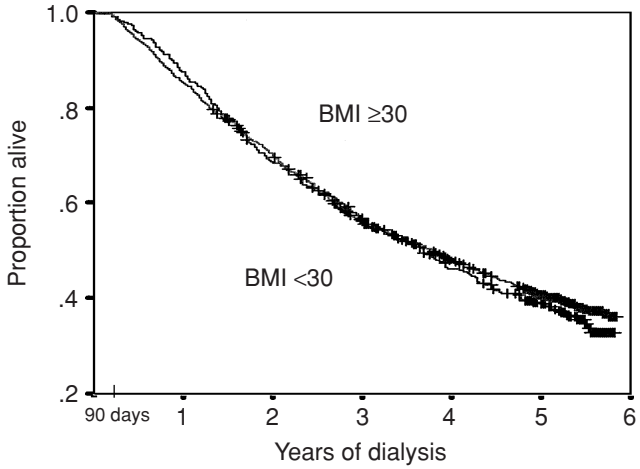

Fig. 7. Kaplan-Meier plot of patient survival by body mass index (BMI) $\geq$30 kg/m^2 or less, peritoneal dialysis patients only, Dialysis Morbidity and Mortality Wave II (DMMS Wave II). Patients with BMI $\geq$30 kg/m^2 did not have improved survival compared to those with lower BMI, $P > 0.05$ by log-rank test.

plot of survival time by quartile of BMI. As shown, only peritoneal dialysis patients in the lowest quartile of BMI were at increased risk of mortality, while peritoneal dialysis patients in BMI second to fourth quartiles had virtually identical risk of death over time. Results of analysis censored for peritoneal dialysis patients who later changed to hemodialysis was essentially the same. Figure 7 (which did not censor on change from peritoneal dialysis to hemodialysis) and Figure 8 (which did censor on change from peritoneal dialysis to hemodialysis) show that, in contrast, the survival of peritoneal dialysis patients with BMI $\geq$30 kg/m^2 was essentially equivalent to that of peritoneal dialysis patients with lower BMI throughout the study, which was unchanged for censoring on change from peritoneal dialysis to hemodialysis.

BMI $\geq$30 kg/m^2 was independently associated with improved survival in Cox regression analysis of the entire cohort of DMMS Wave II patients. However, there was a

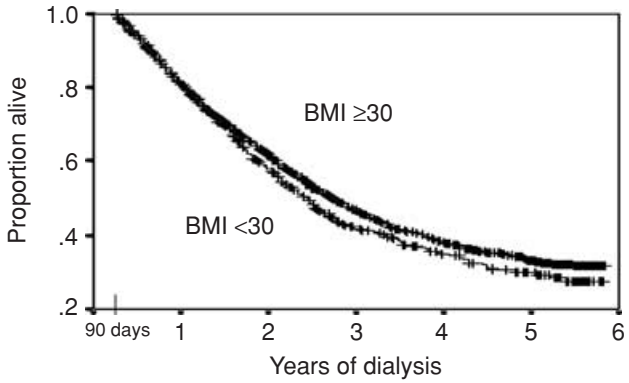

Fig. 8. Analysis from Fig. 7 censored for change to hemodialysis showed a lower rate of death overall, but a similar relationship between BMI and survival.

Table 2. Cox regression of factors associated with mortality (multivariate), hemodialysis patients only

	P value	Adjusted hazards ratio	95% CI
Body mass index ≥*30 kg/m²*	0.042	0.89	0.81, 0.99
Quartiles of body mass index			
<21.9	0.001	1.41	1.15, 1.71
21.9–24.9	0.057	1.21	0.99, 1.46
25.0–29.9	0.61	0.95	0.78, 1.16
>29.9	Reference	1.00	
Age (per 10 years)	<0.0001	1.22	1.17, 1.28
African American race	.003	0.79	0.68, 0.93
Malnutrition	<0.001	1.42	1.17, 1.73
Peripheral vascular disease	0.004	1.28	1.08, 1.51
Coronary heart failure	<0.001	1.39	1.20, 1.61
Serum albumin (per higher quartile)	<0.001	0.84	0.78, 0.89
Independent walking	<0.001	0.73	0.60, 0.88
Renal transplantation (time dependent)	<0.001	0.16	0.09, 0.29
Number in final sample	1295		

Only factors significant in the final model are shown. Interpolated values substituted the mean values for continuous variables with missing values.

significantly adverse interaction between BMI ≥30 kg/m^2 and patients on peritoneal dialysis, such that peritoneal dialysis was a significant modifier of the effect of obesity on survival [$P = 0.001$; adjusted hazard ratio (AHR) 1.41; 95% CI 1.06, 1.88). Therefore, further analysis of the cohort including both peritoneal dialysis and hemodialysis patients was inappropriate, and further analysis was stratified separately for peritoneal dialysis and hemodialysis patients. Other factors significantly associated with mortality in the cohort were similar to those reported previously [14].

Table 2 shows results of Cox regression analysis of factors associated with survival for hemodialysis patients only. In the interpolated model, BMI ≥30 kg/m^2 was significantly associated with improved survival, although only at the margin of statistical significance. Factors that were associated with reduced mortality were use of calcium channel blockers, higher serum albumin levels, and renal transplantation. Older age, malnutrition, peripheral vascular disease, coronary heart disease, congestive heart failure, and use of a temporary catheter were associated with increased mortality. When BMI was assessed as quartiles, hemodialysis patients in the lowest quartile of BMI were at independently greater risk of mortality compared to those in the highest quartile of BMI. In the noninterpolated model, BMI ≥30 kg/m^2 was not significantly associated with reduced mortality in this cohort ($P = 0.08$ in Cox regression).

Table 3 shows results of Cox regression analysis of factors associated with survival for peritoneal dialysis patients only. When BMI was assessed as quartiles, peritoneal dialysis patients in the lowest quartile of BMI were at independently greater risk of mortality compared to those in the highest quartile of BMI. Use of interpolated values did not affect the significance of BMI for peritoneal dialysis patients. In analysis using survival values censored for change of modality to hemodialysis, however, peritoneal dialysis patients in the lowest quartile of BMI were no longer at independently increased risk of morality compared to those in the highest quartile of BMI, as shown in the right columns. No other quartiles of BMI were significantly associated with mortality in comparison with the highest quartile of BMI.

There were no significant interactions between BMI and either race or gender. In stratified analysis limited to patients with BMI ≥30 kg/m^2 (total number in model = 519), peritoneal dialysis (vs. hemodialysis) was not significantly associated with mortality (AHR 1.23; 95% CI 0.82, 1.85; $P = 0.31$), and there was no significant interaction between peritoneal dialysis and diabetes.

DISCUSSION

The present study shows that low BMI was independently associated with increased risk of death regardless of dialysis modality. However, the association between high BMI and survival in chronic dialysis patients differs significantly by dialysis modality. While there were many differences in the characteristics of hemodialysis and peritoneal dialysis patients, most differences were clinically modest even if statistically significant, consistent with previous reports [23–25]. As shown in Figures 3 to 8 and as a significant interaction term with BMI in Cox regression analysis, peritoneal dialysis was an independent effect modifier of the association between obesity with survival. This can be interpreted as meaning that any potentially beneficial association between obesity and survival is less likely in peritoneal dialysis patients than in hemodialysis patients, and that the association of BMI with mortality should be presented separately for hemodialysis and peritoneal dialysis patients, in agreement with previous reports of the entire USRDS

Table 3. Cox regression of factors associated with mortality (multivariate), peritoneal dialysis patients only

	Survival not censored on change to hemodialysis			Survival censored on change to hemodialysis		
	P value	Adjusted hazards ratio	95% CI	*P* value	Adjusted hazards ratio	95% CI
Body mass index ≥30 kg/m^2	0.89	0.99	0.86, 1.15	0.77	1.03	0.86, 1.22
Quartiles of BMI						
<22.4	0.012	1.32	1.07, 1.65	0.36	1.12	0.88, 1.42
22.4–25.7	0.98	1.00	0.81, 1.23	0.26	0.88	0.69, 1.11
>25.7–29.5	0.79	1.03	0.83, 1.27	0.52	0.93	0.74, 1.16
>29.5	Reference	1.00		Reference	1.00	
Number in final sample	1274					

Both models also adjusted for age, race (African American versus all others), gender, use of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, aspirin, calcium channel blockers, angiotensin-converting enzyme inhibitors, serum hemoglobin, serum albumin, diabetes, malnutrition (as a subjective diagnosis), prior history of congestive heart failure and ischemic heart disease, smoking history, and renal transplantation as a time-dependent variable (models were also performed censoring for the date of renal transplantation, with results not substantially different from those shown above).

Interpolated values substituted the mean values for continuous variables with missing values.

population. We report that this finding persists in longer follow-up and adjusting for other important factors that might confound associations with survival, including pertinent laboratory and blood pressure data, medication use, and change of dialysis modality. We found that peritoneal dialysis (vs. hemodialysis) was not significantly associated with mortality in obese dialysis patients, although sample size was relatively small for this subgroup.

The association between BMI and survival in hemodialysis patients has been widely studied. Reports for peritoneal dialysis have been less numerous. Two previous studies, by Johnson et al [8] and Aslam et al [7], apparently contradicted each other, perhaps due to differences in study design. While both previous studies used BMI categories derived from the general population, weight categories may be useful only for comparing the relationship between BMI and survival in the general population with patients on dialysis, and for modeling an association between BMI and survival among dialysis populations. This is the reason we used quartiles of BMI in addition to a priori categorizations of obesity in the present study. In the study of Johnson et al [8], a BMI ≥27.5 was associated with an AHR of 0.09 (95% CI 0.01, 0.85) for mortality in comparison to patients with a lower BMI. This is more than a tenfold lower adjusted risk of mortality, which was certainly not seen in the present study, and is difficult to explain based on clinical experience.

Regardless of initial dialysis modality, any protective effect of obesity on survival is not apparent after renal transplantation [26], and obese dialysis patients have improved survival after renal transplantation [17]. This suggests a direct effect of dialysis modality on the association between obesity and survival.

Why would survival of obese patients differ by dialysis modality? It appears that low BMI is associated with increased mortality in both hemodialysis and peritoneal dialysis, despite the finding of most studies that such patients have higher dialysis adequacy [27, 28]. Therefore, the specific question is, why would obesity be beneficial in hemodialysis but not peritoneal dialysis? Obese patients may be more likely underdialyzed on peritoneal dialysis than on hemodialysis. In fact, body size has been a limiting factor for consideration of peritoneal dialysis as a choice of modality, although no firm "cutoff" size is now specified in current Kidney/Dialysis Outcomes Quality Initiative (K/DOQI) guidelines, so long as patients achieve measured adequacy, which appears possible for obese peritoneal dialysis patients [29]. Although the importance of achieving adequacy has been brought into question by the recent ADEMEX study [30], the lack of adequate data on dialysis adequacy for most patients in the DMMS Wave II cohort is a definite limitation of the current study. While the ADEMEX and HEMO studies [31], of peritoneal dialysis and hemodialysis, respectively, were both landmark clinical trials, each had disproportionately few obese patients. Each also contradicted findings from previous observational trials. It has been very difficult to show an impact of peritoneal dialysis adequacy (nonrenal), or body size, or in fact of any factor except residual renal function on survival of peritoneal dialysis patients [32–34], a dilemma that continues to defy explanation. Some authors have speculated on different mechanisms of malnutrition in patients with chronic kidney disease, namely "uremic" malnutrition and "inflammatory" malnutrition associated with prevalent cardiovascular disease [35]. Whether these factors differ by dialysis modality has not been established. Hemodialysis has been associated with increased inflammatory activity [36, 37]. However, it is difficult to compare markers of inflammation, such as C-reactive protein (CRP), between peritoneal dialysis and hemodialysis because of the dramatic effect of the timing of hemodialysis and intercurrent events (such as vaccinations) on such markers [38]. Unfortunately, anthropometric measures correlate poorly with inflammatory cytokines in hemodialysis patients [39].

Comparisons of survival between hemodialysis and peritoneal dialysis must carefully account for differences in baseline comorbid conditions, as emphasized in previous reports [10, 24], as well as account for possible changes in modality-associated mortality over time [40]. Limitations of the DMMS Wave II database in comparison to other cohorts such as the CHOICE cohort [41] have been noted. We were unable to follow changes in variables over time. Therefore, we could not follow changes in blood pressure, laboratory values, or dialysis adequacy. This most especially applied to possible changes in medication use and changes in patient dry weight. Because such a high proportion (45%) of peritoneal dialysis patients changed modality during the course of the study, calculation of survival time was subject to potential bias, whether or not patients were censored at the time of changing modality to hemodialysis. Bias attributable to not censoring on change to hemodialysis included potentially differing effects of hemodialysis on mortality once modality was changed. However, bias could also be introduced by censoring patients upon change to hemodialysis. Such patients would most likely have had substantial declines in residual renal function, frequent bouts of peritonitis, or other conditions that would place them at risk of increased mortality. It is possible that these conditions were directly attributable to peritoneal dialysis as a modality, although the DMMS Wave II database could not ascertain this with certainty. Therefore, censoring of these patients removed a substantial number of patients who died prematurely. In fact, in analysis censoring peritoneal dialysis patients upon change to hemodialysis, patients with low BMI were no longer independently at increased risk of death, possibly due to the bias described above. However, in both methods of estimating survival times, a high BMI had a neutral association with mortality in peritoneal dialysis patients, which strengthens the finding of this association. We would emphasize that these findings are only associations, and should not be construed to be causative. As mentioned previously, both the HEMO and ADEMEX trials contradicted earlier observational trials; however, it is unlikely the HEMO or ADEMEX trials would have been performed in the absence of those observational trials.

However, DMMS Wave II has some unique advantages. BMI could be calculated from postdialysis weights for hemodialysis patients and on weights 60 days after the start of dialysis for all patients; as such, they may more accurately reflect patient "dry" weight than weights obtained at presentation to ESRD, as reported in CMS Form 2728 (the Medical Evidence Form). Pulse pressure, not available from the Medical Evidence Form, has also been an independent predictor of mortality in other studies of hemodialysis patients [15], but not in peritoneal dialysis patients [42]. Differences in blood pressure patterns and their possible impact on residual renal function may in part be responsible. In addition, medication use, also not available from the Medical Evidence Form, has also been independently associated with survival in this cohort [13, 14]. As far as we are aware, previous studies assessing the impact of BMI and dialysis modality on survival have not assessed for all these factors.

CONCLUSION

Patients with low BMI are at increased risk of death regardless of dialysis modality. However, the relationship between obesity and survival differs by dialysis modality for reasons that have yet to be determined. In fact, obesity has a neutral impact on survival among peritoneal dialysis patients, in contrast to its beneficial association in hemodialysis patients; conversely, among obese dialysis patients, peritoneal dialysis is associated with a higher, but statistically insignificant, risk of mortality.

NOTE ADDED IN PROOF

We would like to acknowledge the recent paper by Syder et al (*Kidney Int* 64:1838–1844, 2003), which performed an analysis of the relationship between BMI and survival among PD patients for the entire population of U.S PD patients from 1995 to 2000. Our results are actually quite similar, and we would emphasize that the survival advantage associated with obesity among PD patients the authors concluded from their study was only seen in the first year of dialysis, not unlike our Figures 5–7, and that this advantage, while statistically significant (relative risk of 0.89). Study design differences between the Snyder et al study and ours are, of course, emphasized in our discussion.

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